

PCTWORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : A61K 39/395, 38/17, 31/57, 31/445, 38/13 // (A61K 39/395, 38:13) (A61K 39/395, 31:57) (A61K 39/395, 31:445) (A61K 38/17, 38:13) (A61K 38/17, 31:57) (A61K 38/17, 31:445)		A1	(11) International Publication Number: WO 98/52606 (43) International Publication Date: 26 November 1998 (26.11.98)
(21) International Application Number: PCT/US98/10075 (22) International Filing Date: 15 May 1998 (15.05.98) (30) Priority Data: 60/046,791 17 May 1997 (17.05.97) US 60/049,389 11 June 1997 (11.06.97) US Not furnished 12 May 1998 (12.05.98) US (63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Applications US Not furnished (CON) Filed on 12 May 1998 (12.05.98) US 60/046,791 (CON) Filed on 17 May 1997 (17.05.97) US 60/049,389 (CON) Filed on 11 June 1997 (11.06.97) (71) Applicant (for all designated States except US): BIOGEN, INC. [-/US]; 14 Cambridge Center, Cambridge, MA 02142 (US).		(72) Inventors; and (75) Inventors/Applicants (for US only): KIRK, Allan, D. [-/US]; Madison, WI (US). HARLAN, David, M. [-/US]; Bethesda, MD (US). THOMAS, David [-/US]; Houston, TX (US). KAUFFMAN, Michael [-/US]; Jamaica Plain, MA 02139-4618 (US). BURKLY, Linda [-/US]; West Newton, MA 02165 (US). (74) Agent: FENTON, Gillian, M.; Biogen, Inc., 14 Cambridge Center, Cambridge, MA 02142 (US). (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i>	
(54) Title: USE OF A CD40:CD154 BINDING INTERRUPTOR TO PREVENT COUNTER ADAPTIVE IMMUNE RESPONSES, PARTICULARLY GRAFT REJECTION			
(57) Abstract <p>Compositions and methods disclosed herein capitalize on the discovery that rejection of a tissue graft can be inhibited using a CD40:CD154 binding interruptor, either alone or in combination with another immunomodulator or immunosuppressor. An advantageous, synergistic combination includes a CD40:CD154 binding interruptor and a CD28 signalling interruptor. An exemplary CD40:CD154 binding interruptor is an anti-CD154 monoclonal antibody, such as an antibody having the antigen-specific binding characteristics of the 5c8 monoclonal antibody. An exemplary CD28 signalling interruptor is a CTLA4-Ig fusion protein. The disclosed compositions and methods unexpectedly can be used to prolong survival of grafted tissue in a recipient host, to reverse acute graft rejection, and to attenuate immunological consequences of the failure of grafted tissue.</p>			